UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,405	01/24/2002	Laurence J. Zwiebel	N7841 DWS	2561

36536 7590 04/08/2005

WYATT, TARRANT & COMBS, LLP
1715 AARON BRENNER DRIVE
SUITE 800
MEMPHIS, TN 38120-4367

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,405	ZWIEBEL, LAURENCE J.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 January 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/24/02, 6/11/02, 8/1/02, 2/17/04, 9/28/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignment*.

Election/Restrictions

1. Applicant's election of Group IV, claims 18-21, drawn polypeptides of SEQ ID NO:2 in the reply filed on 18 January 2005 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP §818.03(a)).

2. The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, and/or Claims

3. The Amendment filed 18 January 2005 has been entered in full. Claims 1-17 and 22-85 have been cancelled, and claims 18-21 are currently pending.

Information Disclosure Statement

4. The information disclosure statements (IDS) filed 24 April 2002, 11 June 2002, 01 August 2002, 17 February 2004, and 28 September 2004 have been considered by the examiner. It is noted that should this application issue as a patent, reference AA (co-pending application for which the Applicant is the sole Inventor) of the IDS filed 01 August 2002 will become public information.

Drawings

5. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R.§§1.821-1.825 will be published as part of the patent. Therefore, it is unnecessarily redundant to repeat the sequence information in the form of

Figures. Applicants should amend the specification to delete any Figures (e.g. Figures 1, 2, 3b, 4b, 5b, 6b, 9b, 10b, and 11b) which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s) and should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO:.

Specification

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Mosquito Arrestin 1 polypeptide".

Claim Rejections - 35 USC § 101 and 35 USC §112, 1st Paragraph

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 18-21 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established

utility. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility.

9. The instant application discloses a nucleic acid set forth as SEQ ID NO:1 that encodes the protein set forth as SEQ ID NO:2. The specification asserts that SEQ ID NO:2 is an arrestin based on a conserved Src homology 3 binding site (See page 24, lines 15-17) and a high degree of homology to known Drosophila sequences (See page 33, lines 1-3). The instant specification does not teach any physiologic ligands or functional characteristics of the arrestin 1 set forth in SEQ ID NO:2 or encoded by the disclosed nucleic acid set forth in SEQ ID NO:1. There is no well-established utility for a specific nucleic acid or amino acid sequence and the specification fails to disclose a specific and substantial utility for the claimed invention.

10. The specification asserts the following as patentable utilities for the claimed arrestin 1 protein of SEQ ID NO:2:

> 1) to screen for compounds that modulate arrestin 1-odorant receptor interactions (pg 5, lines 10-16; pg 24, lines 13-15).

11. This asserted utility is not substantial because it does not reasonably confirm a "real world" context of use. The specification does not identify any of the biological functions that are associated with the claimed molecules. Without the identification of any biological activity or link to a behavioral or physiological consequence associated with the claimed arrestin 1 protein, such constitutes further research to determine the properties of the claimed arrestin 1 protein or conservatively modified or partial peptides, which is insufficient to meet the requirement of 35 USC § 101.

12. The asserted activities and functions are conjectural and are based solely on the identification of the putative protein of SEQ ID NO:2 as being an arrestin. While it is credible that SEQ ID NO:2 is an arrestin, its identification as such is not sufficient to establish either a well known, or a specific, substantial and credible utility. There is no GPCR identified to which it binds, no ligand identified that binds to it, no signaling pathway with which it is involved, and no behavioral or physiological consequence correlated with the polypeptide. The specification asserts that molecules that interfere with interaction between the claimed arrestin protein and its undisclosed receptor, will interfere with mosquito olfactory systems and will thus inhibit mating and feeding having a significant impact on mosquito populations and is helpful, for example, in nuisance and disease vector control for humans and livestock. However, the Instant Application has not established a nexus between the arrestin 1 protein of SEQ ID NO:2 and mosquito olfaction, nor has it established that interfering with the interaction of the claimed arrestin 1 protein with an odorant receptor will have the desired effect of interfering with mosquito olfaction. Since the asserted utility is not present in a ready to use, real-world application, and since significant further research would be required of the skilled artisan to determine how the claimed polypeptide is involved in any activities, the asserted utility is not substantial.

13. The art teaches that the beta arrestins show a high degree of homology between each other as well as to visual arrestins. The art also teaches that B-arrestin 1 and B-arrestin 2, for example, have overlapping, but not identical, functions in both GPCR signaling and internalization. For example, in studies of second-messenger generation using mouse embryo fibroblasts (MEFs) obtained from embryos that lack B-arrestin 1, B-arrestin 2, or both proteins,

cyclic AMP accumulation stimulated by B_2-adrenoceptor activation was enhanced in MEFs lacking one or the other B-arrestins, but was even more robustly enhanced in cells lacking both B-arrestins. Similarly, it was also shown that MEFs expressing the angiotensin AT_{1a} receptor, inositol phosphate accumulation elicited by angiotensin application was only modestly enhanced in the single knockouts, but was robustly enhanced in the double knockout MEFs. This suggests that, at least for desensitization of these two receptors, the B-arrestins might be interchangeable (Pierce et al. Classical and new roles of B-arrestins in the regulation of G-protein-coupled receptors. Nature Reviews. 2:727-733, 2001; See page 729, second paragraph).

14. The art also teaches that although mammalian arrestin proteins cooperate with G protein-coupled receptor kinases (GRKs) in receptor desensitization, loss of *C. elegans* arrestin-1 does not disrupt chemosensation (Fukuto et al. G protein-coupled receptor kinase function is essential for chemosensation in *C. elegans*. Neuron 42:581-593, 2004). Similarly, Dolph (Arrestin: roles in the life and death of retinal neurons. The Neuroscientist 8(4):347-355, 2002) teaches that loss of Drosophila arrestin-1 had no effect on visual physiology or photoreceptor integrity.

15. Thus, although the homology of the arrestin family allows identification of such as arrestins, mere homology is not accepted by those of skill in the art as being predictive of function.

16. Taken together, one skilled in the art would not find substantial the assertion that SEQ ID NO:2 could be used in an assay to identity molecules or compounds that interfered with mosquito olfaction. Utility must be in readily available form. It is possible that, after further characterization, this protein might be found to have a patentable utility, in which case proteins

would have a specific utility, or the protein might be found to be associated with a specific behavioral or physiological consequence.

17. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a protein which has undetermined function or biological significance. Until some actual and specific activity or significance can be attributed to the protein identified in the specification as SEQ ID NO:2, the claimed invention is incomplete.

18. Claims 18-21 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make/use the claimed invention.

19. Furthermore, even if the protein of SEQ ID NO:2 were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the claimed invention.

20. Claims 18 and 20 recite an amino acid sequence of conservatively modified SEQ ID NO:2, and claims 18 and 21 recite an amino acid sequence of SEQ ID NO:2, having at least 20 consecutive residues. It is noted that the limitation of "comprising an amino acid sequence of SEQ ID NO:2, having at least 20 consecutive residues", as recited in claims 18 and 21, can be interpreted to mean any polypeptide that is at least 20 residues long and comprises as few as one amino acid residue of SEQ ID NO:2. However, other than the protein of SEQ ID NO:2, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) which portions of SEQ ID NO:2 are critical to the activity of the protein of SEQ ID NO:2 (which is itself unknown); (2) what modifications (e.g., substitutions, deletions, or additions) one can make to SEQ ID NO:2 that will result in protein mutants with the same activity as the protein of SEQ ID NO:2; and (3) any guidance on how to use peptides of SEQ ID NO:2 which would, based on the language of said claims, encompass both active and an extraordinary number of inactive variants of SEQ ID NO:2, especially in the absence of any functional limitations in the claims. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and is unpredictable. Furthermore, it is known in the art that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions (See Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., The Protein Folding Problem and Tertiary Structure Prediction, 1994, pp. 492-495). For example, analysis of deletion mutant of B-arrestin 2 demonstrated that the amino-terminus was required for optimal interaction of B-arrestin 2 with apoptosis signal-related kinase 1

(ASK1) and that the carboxyl-terminus was required for optimal interaction with c-Jun amino-terminus kinase 3 (JNK3) (McDonald et al. B-arrestin 2: a receptor-regulated MAPK scaffold for the activation of JNK3. Science 290:1574-1577, 2000). Similarly, site directed mutagenesis studies on visual arrestin have shown that there are specific regions which are critical to the binding of arrestin with the phosphorylated c-terminus of rhodopsin as well as the ability of arrestin to mobilize secondary binding sites (Gurevich et al. Visual arrestin binding to rhodopsin. The Journal of Biological Chemistry. 270(11):6010-6016, 1995).

21. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of substitutions/deletions on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, even if the protein of SEQ ID NO:2 were found to be enabled.

22. Claims 18-21 are also rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

23. The specification discloses a protein of SEQ ID NO:2 and a nucleic acid sequence of SEQ ID NO:1 that encodes the protein of SEQ ID NO:2. However, claims 18 and 20 recite an amino acid sequence of conservatively modified SEQ ID NO:2, and claims 18 and 21 recite an amino acid sequence of SEQ ID NO:2, having at least 20 consecutive residues. It is noted that the limitation of "comprising an amino acid sequence of SEQ ID NO:2, having at least 20 consecutive residues", as recited in claims 18 and 21, can be interpreted as being any polypeptide that is at least 20 residues long and comprises as few as one amino acid residue of SEQ ID NO:2. The claims do not require that the proteins possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptide molecules.

24. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in claims 18 and 20-21 is a partial structure in the form of a recitation of conservatively modified or "having at least 20 consecutive residues". The specification does not identify any particular structure/function correlation or biological activity. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is the polypeptide set forth as SEQ ID NO:2. Accordingly, the specification does not provide adequate written description of the claimed genus.

25. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

26. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

27. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

28. Therefore, only the polypeptide set forth as SEQ ID NO:2, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

29. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

30. Claims 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Hyde et al. (Twenty *Drosophila* visual system cDNA clones: one is a homolog of human arrestin. Proc. Natl. Acad. Sci. USA. 87:1008-1012, 1990; cited by Applicant).

31. Hyde et al. teach a polypeptide that shares 100% sequence identity to residues 228-247 of SEQ ID NO:2 of the instant application (See attached sequence alignment). It is noted that the limitation of "comprising an amino acid sequence of SEQ ID NO:2, having at least 20 consecutive residues", as recited in claims 18 and 21, can be interpreted as being any polypeptide that is at least 20 residues long and comprises as few as one amino acid residue of SEQ ID NO:2. However, for the purposes of applying art, the phrase "an amino acid sequence of SEQ ID NO:2, having at least 20 consecutive residues", as recited in the claims, has been interpreted to mean an amino acid comprising a sequence that shares 100% identity to at least 20 consecutive residues of SEQ ID NO:2, and thus the claims read on the polypeptide taught by Hyde et al.

Summary

32. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
March 29, 2005

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER